Support for this amendment is found in originally filed claim 8, and in the specification at p. 11, line 19 to p. 12, line 17. No claim was narrowed by these amendments. The Examiner has unilaterally withdrawn claims 11, 12, 18, and 19 from consideration. Applicants traverse this withdrawal; see section V below.

II. Information Disclosure Statement

The Examiner returned the PTO 1449 forms Applicants filed on February 13, 2001. However, the Examiner did not initial several abstracts listed on pages 4 and 5 of the 1449 form, apparently because no date was listed on the 1449 form. However, the publication date is listed on the face of each abstract and on each patent application. Applicants respectfully request that the Examiner initial and return the aforementioned PTO 1449 form to Applicants.

III. Rejections under 35 U.S.C. § 112

The Examiner rejected claims 1 and 22 under 35 U.S.C. § 112, first and second paragraphs. The Examiner argues that R^1 may be a heterocyclic ring containing adjacent O-S, O-O, or S-S heteroatoms, which the Examiner does not believe to exist. Applicants respectfully traverse this rejection.

The Examiner is reminded that even if a claim encompasses inoperative embodiments, the presence of such embodiments does not necessarily constitute a proper basis for rejection. *See e.g. In re Dihn-Nguyen*, 492 F. 2d 856, 858-59 (C.C.P.A 1974) (holding that "[e]ven if some of the claimed combinations were inoperative, the claims are not necessarily invalid.") The deciding factor in this determination is whether the skilled artisan would be able to recognize and avoid such inoperative embodiments. In this respect, the following quotation of the court in *In re Cook* is on point:

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> [M]any patented claims read on vast numbers of inoperative embodiments in the trivial sense that they can, and do, omit 'factors which must be presumed to be within the level of ordinary skill in the art,' and therefore read on embodiments in which such factors *may* be included in such a manner as to make the embodiments inoperative. <u>There is nothing wrong with this so long as it would be obvious to one of ordinary skill in the relevant art how to include those factors in such manner as to make the embodiment operative rather than inoperative.</u>

In re Cook, 439 F. 2d 730,735 (C.C.P.A. 1971)(internal citations omitted, italics in original, underlining added).

The emphasis on whether the skilled artisan would be able to recognize without undue experimentation which embodiments encompassed by the claims are inoperative has been echoed in various court decisions. *See e.g., Atlas Powder Co. v. E.I. duPont de Nemours & Co.*, 750 F. 2d 1569,1577 (Fed. Cir. 1984) (quoting the above-cited passage in *In re Dihn-Nguyen* and even adding that "it is not a function of the claims to specifically exclude...possible inoperative substances...").

In the present case, the skilled artisan would easily recognize any possible unstable heterocycle rings encompassed by claim 1 and would not attempt to prepare them. Indeed, the Examiner, presumed by the courts to be a person of ordinary skill in the art, has readily recognized what he believes represent inoperative embodiments within the scope of the claims. *See. e.g., In re Lee*, 277 F.3d 1338, 1345 (Fed. Cir. 2002) (holding that both the Examiner and the Patent Board of Appeals are presumed to act from the viewpoint of a person having ordinary skill in the art to which the subject matter pertains). Practicing the full scope of the claimed invention, therefore, would not entail undue experimentation.

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The Examiner argues that the definition of heteroaryl in claim 1 is not allowable because it recites "one or more heteroatoms." Office Action at p. 2 (emphasis in original). The Examiner adds that "[t]his claims a [huge] number of compounds that would require specific conception by the reader. [Their] rings would dwarf the pyrimidine of formula I, and control the classification and search, elsewhere." *Id.* Applicants respectfully traverse this rejection.

Applicants do not understand the exact nature of this rejection and respectfully seek clarification from the Examiner in this respect. Applicants assume that this rejection is related to the presence of adjacent O-S, O-O, or S-S heteroatoms in a ring because the Examiner underlined "one or more" heteroatoms above. To the extent that this is the case, Applicants have already responded to this rejection in the preceding section. If the Examiner is arguing that the language of the claim is indefinite and that the skilled artisan would not be able to determine what is meant by "heteroaryl," then Applicants fail to see the source of the confusion because all the terms in the definition of "heteroaryl" are well understood within the art. Accordingly, the scope of the claim is clear, definite, and particularly points out and distinctly claims the subject matter of the invention. The Examiner has provided no arguments as to why the skilled artisan would fail to determine the metes and bounds of the claim.

Furthermore, the specification discloses numerous specific examples of heteroaryl radicals such as: pyrrole, furan, thiophene, imidazole, pyrazole, 1,2,3-triazole, 1,2,4-triazole, 1,3-dioxole, 1,3-oxazole, 1,2-oxazole, 1,3-thiazole, 1,2-thiazole, tetrazole, pyridine, pyridazine, pyrimidine, pyrazine, pyran, thiopyran, 1,4-dioxin, 1-2-oxazine, 1,3-oxazine, 1,4-oxazine, 1,2-thiazine, 1,3-thiazine, 1,4-thiazine, 1,2,3-triazine,

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1,2,4-triazine, 1,3,5-triazine, 1,2,4,5-tetrazine, azepine, 1,2-diazepine, 1,3-diazepine, 1,4-diazepine, 1,3-oxazepine, 1,3-thiazepine, indole, benzothiophene, benzofuran, benzothiazole, benzimidazole, quinoline, isoquinoline, cinnoline, quinazoline, quinoxaline, phthalazine, thienothiophenes, 1,8-naphthyridine, pteridine, or phenothiazine, pyrrolidine, piperidine, perhydroazepine (hexamethyleneimine), piperazine, morpholine, 1,3-thiazolidine, and thiomorpholine. Specification at p. 8, line 26 to p. 9, line 20. In light of the foregoing remarks, Applicants respectfully request that this rejection be withdrawn.

The Examiner rejected claims 13-15 and 20-21 as being dependent on a rejected claim. In light of the foregoing remarks, claim 1 fully complies with 35 U.S.C. § 112 and Applicants respectfully request that this rejection be withdrawn.

The Examiner also rejected claims 10 and 17 under 35 U.S.C. § 112, first and second paragraphs. The Examiner argues that these claims do not indicate their intended use, and that the specification could not support all uses. Applicants respectfully traverse.

Claims 10 and 17 claim simple compositions of matter. Applicants note that nothing in 35 U.S.C. § 112, either first or second paragraphs, requires that composition of matter claims indicate the intended use for the composition *within the claims*. The only statutory requirement for composition claims in this regard is that the claimed compositions have utility. 35 U.S.C. § 101. The specification discloses that the compounds of the invention are useful, for example, in the therapy and prophylaxis of illnesses and pathological conditions associated with low cGMP levels. Specification at p. 16, line 33 to p. 17, line 6. Various specific examples of these illnesses and

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pathological conditions are also listed therein. *Id.* As far as this issue is concerned, claims 10 and 17 do not differ from claims 1 and 5, also composition of matter claims, which the Examiner has not objected to in this respect. Therefore, claims 10 and 17 fully comply with 35 U.S.C. § 112 and Applicants respectfully request that this rejection be withdrawn.

IV. Objections under the Utility Guidelines

The Examiner argues that activating soluble guanylate cyclase is not a real world utility and that this utility does not comply with the Utility Guidelines (PTO Guidelines on Utility Requirements, BNA's Patent and Trademark Journal, 50:295-309 (July 20, 1995)). Applicants respectfully traverse.

The Utility Guidelines clearly state that "a disclosure that identifies a particular biological activity of a compound and explains how that activity can be utilized in a particular therapeutic application of the compound *does contain an assertion of specific utility*." Utility Guidelines at p. 302, paragraph bridging col. 1-2. One embodiment of Applicants' invention indicates that the compounds of the invention "bring about strong guanylate cyclase activation, on account of which they are suitable for the therapy and prophylaxis of illnesses associated with a low cGMP level." Specification at p. 3, line 36 to p. 4, line 2. The specification provides various examples of such illnesses. Specification at page 2, lines 26-35; p. 16, line 33 to p. 17, line 6. Accordingly, activating soluble guanylate cyclase does comply with the utility guidelines and Applicants respectfully request that this objection be withdrawn.

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V. Withdrawal of claims under 37 C.F.R. § 1.499 for lack of unity of invention

The Examiner withdrew claims 11, 12, 18, 19, and 23 under 37 C.F.R. § 1.499 for being directed to more than one utility. Applicants respectfully traverse.

The claims comply with the unity of invention requirement and should be examined together in this application.

Applicants maintain that the pending claims conform to the unity of invention requirement under 37 C.F.R. § 1.475 for the reasons of record. In particular, Applicants identify the property of activating guanylate cyclase by the compounds of the invention as at least one of the unifying technical features between the composition claims and the method-of-use claims as required by § 1.475. Specification at p. 3, line 36 to p. 4, line 2. The Examiner has provided no arguments in response to this assertion by Applicants in the amendment filed on January 16, 2002.

Aside from the unity of invention issue, Applicants should be allowed to elect th subject matter to be examined after proper issuance of a requirement to mak an election of species by the Examiner

Contrary to the Examiner's assertion, M.P.E.P § 806.05(h) does not provide the Examiner with the authority to withdraw claims unilaterally. Section 806.05(h) merely provides guidelines for issuing a restriction requirement between claims directed to a product and claims directed to methods of using that product. The Examiner has not issued a proper restriction/election requirement, which would call for an indication that the claims withdrawn are patentably distinct from the claims being examined or, even if the application includes claims to independent inventions, that search and examination of the entire set of claims in the application cannot be made without a serious burden on the Examiner. M.P.E.P. § 803.

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In light of the Examiner's withdrawal of claims 11, 12, 18, 19, and 23, Applicants elect, with traverse, the subject matter of claim 12 wherein the medical condition is a cardiovascular disorder. Applicants' traversal is based on two separate grounds. First, this application is a PCT application that has entered the U.S. national stage under 35 U.S.C. § 371. Therefore, even if the application contains more than one patentably distinct invention, this application should be examined under the Unity of Invention criteria. 37 C.F.R. § 1.475. The Unity of Invention criteria allows for the examination of separate inventions in the same application as long as there is a unifying technical relationship between those inventions. As argued previously, the present claims comply with the Unity of Invention requirement

Second, Applicants traverse any election/restriction requirement on the grounds that the Examiner has not shown that there would be a **serious** burden to examine all of the claims in the application together, as required by the M.P.E.P. M.P.E.P. § 803.

Even if claims directed to methods of use are withdrawn from consideration, these claims are subject to rejoinder when the product claims are found patentable

Applicants respectfully remind the Examiner that in view of the court findings in *In Re Ochiai*, 71 F.3d 1565 (Fed. Cir. 1995) and *In re Brouwer*, 77 F.3d 422 (Fed. Cir. 1996), claims directed to processes of making or using a novel compound are subject to rejoinder with claims drawn to that novel compound once the compound is found patentable. *See* M.P.E.P. § 2116.01. All of the claims withdrawn by the Examiner are drawn to methods of using the compounds of claim 1. Therefore, pursuant to the above-referenced rejoinder procedure, Applicants respectfully request that all pending claims be examined together in this application.

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VI. Rejections under 35 U.S.C. § 103

The Examiner rejected claim 1 under 35 U.S.C. §103, as being unpatentable over the compounds removed by the proviso at the end of claim I. The Examiner argues that the next adjacent compounds to those removed would be structurally obvious from the compounds removed. Applicants respectfully traverse this rejection.

Foremost, the Examiner inquires: "What is the purpose of the proviso statement on page 5 of the most recent response? Is art being written around? See new Rule 105; 37 CFR 105." Office Action at p. 2. Does this statement represent a formal request of information under 37 C.F.R. § 105? Applicants seek clarification.

The proviso at the end of claim 1 disclaims compounds disclosed in European Patent Application EP 0 555 478, issued to Chokai *et al.*, listed in the Information Disclosure Statement filed on February 13, 2001. *Chokai* was cited by the Examiner in an obviousness rejection of claim 1 in the Office Action dated July 20, 2001.

The Examiner indicates that:"In re Nomiya, 184 USPQ 607, provides that there is no reason not to conclude that the species removed by exception are in the prior art, and reject in view of those species." Office Action at p. 2. Applicants respectfully disagree with the Examiner's interpretation of *In re Nomiya*.

The relevant part of this opinion merely indicates that *express statements* by Applicants regarding what is in the prior art can be used in anticipation or obviousness rejections. *In re Nomiya*, 184 U.S.P.Q. at 611. There is no indication by the court, however, about any presumption that what an applicant chooses to exclude from the scope of the claims is necessarily in the prior art. Furthermore, and contrary to the

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Examiner's assertion, *In re Nomiya* does not provide a basis for making obviousness rejections based on provisos in claims.

The Examiner's position seems to be that the full scope of the proviso in claim 1 is in the prior art. However, Applicants remind the Examiner that in the response filed January 16, 2002, Applicants broadened the proviso in claim 1 in reply to an obviousness rejection of this claim in view of *Chokai*. The Examiner did not repeat that rejection in the present Office Action and, therefore, claim 1 is presumed to be patentable over *Chokai*. *Chokai* is the only relevant prior art of record. Accordingly, *the proviso in claim 1 already includes any compounds allegedly obvious in light of the prior art*. Therefore, none of the compounds disclosed in *Chokai* render unpatentable the subject matter of the present claims. Applicants respectfully request that this rejection be withdrawn.

The Examiner rejected claims 2-8 as being dependent on a rejected claim. In light of the foregoing remarks, claim 1, from which claims 2-8 depend, is not obvious in light of the prior art and Applicants respectfully request that this rejection be withdrawn.

The Examiner rejected claim 15 as "an obvious process of producing compounds of claim 5, that is the same process of claim 8. Claim 15 is rejected as a duplicate of claim 8. The process, itself, is what is being claimed, and is identical." Office Action at p. 4. Applicants respectfully traverse this rejection.

Applicants respectfully remind the Examiner that when interpreting a claimed invention, the invention as a whole must be considered. M.P.E.P § 2142.02. Furthermore, "[i]nterpreting a claimed invention as a whole requires consideration of all claim limitations." M.P.E.P. § 2116.01. Therefore, claims 8 and 15 are not identical

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because they depend from claims 1 and 5 respectively, which are different in scope. Accordingly, Applicants respectfully request that this rejection be withdrawn.

The Examiner rejected claims 8 and 15 as being unpatentable under 35 U.S.C. § 103. The Examiner argues that "the vague nature of activating 4-hydroxy pyrimidine in claim 8 could include converting the hydroxy to a chloro as noted on page 84 of EP 055693, of record. The reaction of the resulting (activated) compound with a nitrogen containing compound with the elimination of HCl, is shown on page 27 of WO 98/370179, of record." Office Action at paragraph bridging p. 4-5. Applicants respectfully traverse this rejection.

From the above statement, Applicants understand that the Examiner is not analyzing all of the limitations in claims 8 and 15 when comparing these claims to the prior art. The Patent and Trademark Office's examination guidelines clearly indicate that an otherwise conventional process could be patented if it is limited to making or using a nonobvious product. M.P.E.P. § 2116.01. Because the compounds of claims 1 and 5 are patentable over the prior art, the processes of making and using them (claims 8, 11, 12, 15, 18-19, and 21-23) are also patentable over the prior art. Accordingly, Applicants respectfully request that this rejection be withdrawn.

VII. Conclusions

In view of the foregoing amendments and remarks, Applicants respectfully request the examination of this application and the timely allowance of the pending claims.

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If there is any fee due in connection with the filing of this Preliminary Amendment, please charge the fee to our Deposit Account No. 06-0916.

Respectfully submitted,

FINNEGAN, HENDERSON, FARABOW, GARRETT & DUNNER, L.L.P.

By: _____
Carlos M. Tellez
Reg. No. 48,638

Dated: June 10, 2002

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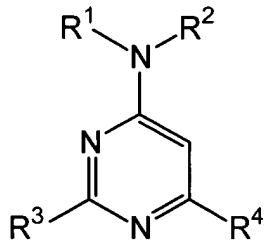
Appendix to Response and Amendment dated June 10, 2002

1. A compound of the formula I,



I

in which

R^1 is $(C_1\text{-}C_8)$-alkyl, which can be substituted by one or more identical or different substituents chosen from hydroxyl, $(C_1\text{-}C_4)$-alkoxy, $(C_1\text{-}C_4)$-alkyl-$S(O)_m$-, R^5R^6N and aryl; $(C_3\text{-}C_9)$-cycloalkyl, which can be substituted by one or more identical or different substituents chosen from $(C_1\text{-}C_4)$-alkyl, hydroxyl and amino; or a radical of a 5-membered to 7-membered saturated heterocyclic ring that contains one or two identical or different hetero ring members chosen from O, NR^7 and $S(O)_m$ and that can be substituted by one or more identical or different substituents chosen from $(C_1\text{-}C_4)$-alkyl and aryl-$(C_1\text{-}C_4)$-alkyl-;

and

R^2 is hydrogen, $(C_1\text{-}C_8)$-alkyl, which can be substituted by one or more identical or different substituents chosen from hydroxyl, $(C_1\text{-}C_4)$-alkoxy, $(C_1\text{-}C_4)$-alkyl-$S(O)_m$-, R^5R^6N and aryl; $(C_3\text{-}C_9)$-cycloalkyl, which can be substituted by one or more identical or different substituents chosen from $(C_1\text{-}C_4)$-

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alkyl, hydroxyl and amino; or the radical of a 5-membered to 7-membered saturated heterocyclic ring that contains one or two identical or different hetero ring members chosen from O, NR^7 and $S(O)_m$ and that can be substituted by one or more identical or different substituents chosen from (C_1-C_4)-alkyl and aryl-(C_1-C_4)-alkyl-; or

R^1R^2N is a radical, bonded via a ring nitrogen atom, of a 5-membered to 7-membered saturated heterocyclic ring that, in addition to the nitrogen atom carrying the radicals R^1 and R^2, can contain a further hetero ring member chosen from O, NR^7 and $S(O)_m$ and that can be substituted by one or more identical or different substituents chosen from (C_1-C_4)-alkyl, hydroxyl, (C_1-C_4)-alkoxy, R^8R^9N, hydroxycarbonyl, (C_1-C_4)-alkoxycarbonyl and R^8R^9N-CO-;

R^3 is phenyl, which can be substituted by one or more identical or different substituents chosen from halogen, (C_1-C_4)-alkyl, phenyl, CF_3, NO_2, OH, -O-(C_1-C_4)-alkyl, -O-(C_2-C_4)-alkyl-O-(C_1-C_4)-alkyl, (C_1-C_2)-alkylenedioxy, NH_2, -NH-(C_1-C_4)-alkyl, N((C_1-C_4)-alkyl)$_2$, -NH-CHO, -NH-CO-(C_1-C_4)-alkyl, -CN, -CO-NH_2, -CO-NH-(C_1-C_4)-alkyl, -CO-N((C_1-C_4)-alkyl)$_{-2}$, -CO-OH, -CO-O-(C_1-C_4)-alkyl, -CHO and –CO-(C_1-C_4)-alkyl;

R^4 is (C_2-C_5)-alkyl, trifluoromethyl or phenyl, which can be substituted by one or more identical or different substituents chosen from halogen, (C_1-C_4)-alkyl, phenyl, CF_3, NO_2, OH, -O-(C_1-C_4)-alkyl, -O-(C_2-C_4)-alkyl-O-(C_1-C_4)-alkyl, (C_1-C_2)-alkylenedioxy, NH_2, -NH-(C_1-C_4)-alkyl, N((C_1-C_4)-alkyl$_2$, -NH-CHO, -NH-CO-(C_1-C_4)-alkyl, -CN, -CO-NH_2, -CO-NH-(C_1-C_4)-alkyl, -CO-N((C_1-C_4)-alkyl$_2$, -CO-OH, -CO-O-(C_1-C_4)- alkyl, -CHO and –CO-(C_1-C_4)-alkyl;

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R^5 and R^6 are identical or different radicals chosen from hydrogen and $(C_1$-$C_4)$-alkyl; or the group R^5R^6N is a radical, bonded via a ring nitrogen atom, of a 5-membered to 7-membered saturated or ~~saturated~~ **unsaturated** heterocyclic ring that, in addition to the nitrogen atom carrying the radicals R^5 and R^6, can additionally contain as a further hetero ring member an oxygen atom, a group $S(O)_m$ or a nitrogen atom and that can carry on ring carbon atoms one or more identical or different substituents chosen from $(C_1$-$C_4)$-alkyl, hydroxyl and amino and that can carry on a ring nitrogen atom a radical R^7;

R^7 is hydrogen, $(C_1$-$C_4)$-alkyl, aryl-$(C_1$-$C_4)$-alkyl-, hydroxy-$(C_1$-$C_4)$-alkyl, hydroxycarbonyl-$(C_1$-$C_4)$-alkyl-, $((C_1$-$C_4)$-alkoxycarbonyl)-$(C_1$-$C_4)$-alkyl, R^8R^9N-CO-$(C_1$-$C_4)$-alkyl-, R^{10}-SO_2- or aryl; where R^7, if this group is present on a piperazino radical representing R^1R^2N, cannot be carbocyclic aryl or carbocyclic aryl-$(C^1$-$C^4)$-alkyl;

R^8 and R^9 are identical or different radicals chosen from hydrogen and $(C_1$-$C_4)$-alkyl;

R^{10} is $(C_1$-$C_4)$-alkyl, aryl or R^8R^9N;

aryl is phenyl, naphthyl or heteroaryl, all of which can be substituted by one or more identical or different substituents chosen from halogen, $(C_1$-$C_4)$-alkyl, phenyl, CF_3, NO2, OH, -O-$(C_1$-$C_4)$-alkyl, O-$(C_2$-$C_4)$-alkyl-O-$(C_1$-$C_4)$-alkyl, $(C_1$-$C_2)$-alkylenedioxy, NH_2, -NH-$(C_1$-$C_4)$-alkyl, -N($(C_1$-$C_4)$-$alkyl_2$, -NH-CHO, -NH-CO-$(C_1$-$C_4)$-alkyl, -CN, CO-NH_2, -CO-NH-$(C_1$-$C_4)$-alkyl, -CO-

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$N((C_1-C_4)\text{-alkyl}_2$, -CO-OH, -CO-O-$(C_1-C_4)$-alkyl, -CHO and –CO-$(C_1-C_4)$-alkyl;

heteroaryl is the radical of a monocyclic 5-membered or 6-membered aromatic heterocycle or of a bicyclic 8-membered to 10-membered aromatic heterocycle, each of which contains one or more identical or different ring heteroatoms chosen from N, O and S;

m is 0, 1 or 2;

or a stereoisomeric form of a compound of formula I,

or a mixture of stereoisomeric forms of compounds of formula I in all ratios,

or a physiologically tolerable salt of a compound of formula I,

or a physiologically tolerable salt of a stereoisomeric form of a compound of formula I;

compounds of the formula I being excluded in which, simultaneously, R^4 is ethyl, tert-butyl, or trifluoromethyl; R^3 is phenyl, which can be substituted by one or two identical or different substituents chosen from halogen, OH, -O-R^{11} and CF_3, R^1R^2N is R^{11} -NH-, $(R^{11})_2N$- or $R^{12}R^{13}N$-$(CH_2)_p$-NH-; p is 2 or 3; R^{11} is saturated unsubstituted (C_1-C_4)-alkyl; and R^{12} and R^{13} are identical or different radicals chosen from hydrogen and R^{11} or the group $R^{12}R^{13}N$ is a radical, bonded via a ring nitrogen atom, of a 5-membered or 6-membered saturated heterocyclic ring that, in addition to the nitrogen atom carrying the radicals R^{12} and R^{13}, can additionally contain as a further hetero ring member an oxygen atom, a sulfur

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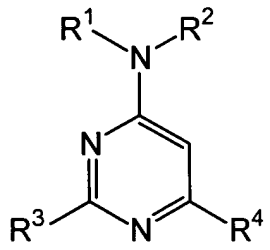
atom or a nitrogen atom and that can be substituted by an aryl substituted by one or two identical or different substituents chosen from halogen, OH, -O-R^{11}, and CF_3.

15. A process for the preparation of at least one compound of claim 5, which comprises activating a 4-hydroxypyrimidine of the formula IV and then reacting it with an amine of a formula VI;

and optionally reacting the resulting product with a suitable reagent to form a pharmaceutically acceptable salt.

22. A method of treating a cardiovascular disorder, comprising administering to a patient in need thereof an effective amount of at least one compound of formula I,



I

in which

R^1 is (C_1-C_8)-alkyl, which can be substituted by one or more identical or different substituents chosen from hydroxyl, (C_1-C_4)-alkoxy, (C_1-C_4)-alkyl-$S(O)_m$-, R^5R^6N and aryl; (C_3-C_9)-cycloalkyl, which can be substituted by one or more identical or different substituents chosen from (C_1-C_4)-alkyl, hydroxyl and amino; or a radical of a 5-membered to 7-membered saturated heterocyclic ring that contains one or two identical or different hetero ring members chosen from O, NR^7 and $S(O)_m$ and that can be substituted by

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one or more identical or different substituents chosen from $(C_1\text{-}C_4)$-alkyl and aryl-$(C_1\text{-}C_4)$-alkyl-;

and

R^2 is hydrogen, $(C_1\text{-}C_8)$-alkyl, which can be substituted by one or more identical or different substituents chosen from hydroxyl, $(C_1\text{-}C_4)$-alkoxy, $(C_1\text{-}C_4)$-alkyl-$S(O)_m$-, R^5R^6N and aryl; $(C_3\text{-}C_9)$-cycloalkyl, which can be substituted by one or more identical or different substituents chosen from $(C_1\text{-}C_4)$-alkyl, hydroxyl and amino; or the radical of a 5-membered to 7-membered saturated heterocyclic ring that contains one or two identical or different hetero ring members chosen from O, NR^7 and $S(O)_m$ and that can be substituted by one or more identical or different substituents chosen from $(C_1\text{-}C_4)$-alkyl and aryl-$(C_1\text{-}C_4)$-alkyl-; or

R^1R^2N is a radical, bonded via a ring nitrogen atom, of a 5-membered to 7-membered saturated heterocyclic ring that, in addition to the nitrogen atom carrying the radicals R^1 and R^2, can contain a further hetero ring member chosen from O, NR^7 and $S(O)_m$ and that can be substituted by one or more identical or different substituents chosen from $(C_1\text{-}C_4)$-alkyl, hydroxyl, $(C_1\text{-}C_4)$-alkoxy, R^8R^9N, hydroxycarbonyl, $(C_1\text{-}C_4)$-alkoxycarbonyl and R^8R^9N-CO-;

R^3 is phenyl, which can be substituted by one or more identical or different substituents chosen from halogen, $(C_1\text{-}C_4)$-alkyl, phenyl, CF_3, NO_2, OH, -O-$(C_1\text{-}C_4)$-alkyl, -O-$(C_2\text{-}C_4)$-alkyl-O-$(C_1\text{-}C_4)$-alkyl, $(C_1\text{-}C_2)$-alkylenedioxy, NH_2, -NH-$(C_1\text{-}C_4)$-alkyl, N($(C_1\text{-}C_4)$-alkyl)$_2$, -NH-CHO, -NH-CO-$(C_1\text{-}C_4)$-alkyl, -CN, -CO-NH_2, -CO-NH-$(C_1\text{-}C_4)$-alkyl, -CO-N($(C_1\text{-}C_4)$-alkyl)$_2$, -CO-OH, -CO-O-$(C_1\text{-}C_4)$-alkyl, -CHO and –CO-$(C_1\text{-}C_4)$-alkyl;

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R^4 is (C_2-C_5)-alkyl, trifluoromethyl or phenyl, which can be substituted by one or more identical or different substituents chosen from halogen, (C_1-C_4)-alkyl, phenyl, CF_3, NO_2, OH, -O-(C_1-C_4)-alkyl, -O-(C_2-C_4)-alkyl-O-(C_1-C_4)-alkyl, (C_1-C_2)-alkylenedioxy, NH_2, -NH-(C_1-C_4)-alkyl, N$((C_1-C_4)$-alkyl$_2$, -NH-CHO, -NH-CO-(C_1-C_4)-alkyl, -CN, -CO-NH_2, -CO-NH-(C_1-C_4)-alkyl, -CO-N$((C_1-C_4)$-alkyl$_2$, -CO-OH, -CO-O-(C_1-C_4)- alkyl, -CHO and –CO-(C_1-C_4)-alkyl;

R^5 and R^6 are identical or different radicals chosen from hydrogen and (C_1-C_4)-alkyl; or the group R^5R^6N is a radical, bonded via a ring nitrogen atom, of a 5-membered to 7-membered saturated or ~~saturated~~ **unsaturated** heterocyclic ring that, in addition to the nitrogen atom carrying the radicals R^5 and R^6, can additionally contain as a further hetero ring member an oxygen atom, a group $S(O)_m$ or a nitrogen atom and that can carry on ring carbon atoms one or more identical or different substituents chosen from (C_1-C_4)-alkyl, hydroxyl and amino and that can carry on a ring nitrogen atom a radical R^7;

R^7 is hydrogen, (C_1-C_4)-alkyl, aryl-(C_1-C_4)-alkyl-, hydroxy-(C_1-C_4)-alkyl, hydroxycarbonyl-(C_1-C_4)-alkyl-, $((C_1-C_4)$-alkoxycarbonyl)-(C_1-C_4)-alkyl, R^8R^9N-CO-(C_1-C_4)-alkyl-, R^{10}-SO_2- or aryl; where R^7, if this group is present on a piperazino radical representing R^1R^2N, cannot be carbocyclic aryl or carbocyclic aryl-(C^1-C^4)-alkyl;

R^8 and R^9 are identical or different radicals chosen from hydrogen and (C_1-C_4)-alkyl;

R^{10} is (C_1-C_4)-alkyl, aryl or R^8R^9N;

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aryl is phenyl, naphthyl or heteroaryl, all of which can be substituted by one or more identical or different substituents chosen from halogen, (C_1-C_4)-alkyl, phenyl, CF_3, NO2, OH, -O-(C_1-C_4)-alkyl, O-(C_2-C_4)-alkyl-O-(C_1-C_4)-alkyl, (C_1-C_2)-alkylenedioxy, NH_2, -NH-(C_1-C_4)-alkyl, -N((C_1-C_4)-alkyl$_2$, -NH-CHO, -NH-CO-(C_1-C_4)-alkyl, -CN, CO-NH_2, -CO-NH-(C_1-C_4)-alkyl, -CO-N((C_1-C_4)-alkyl$_2$, -CO-OH, -CO-O-(C_1-C_4)-alkyl, -CHO and –CO-(C_1-C_4)-alkyl;

heteroaryl is the radical of a monocyclic 5-membered or 6-membered aromatic heterocycle or of a bicyclic 8-membered to 10-membered aromatic heterocycle, each of which contains one or more identical or different ring heteroatoms chosen from N, O and S;

m is 0, 1 or 2;

or a stereoisomeric form of a compound of formula I,

or a mixture of stereoisomeric forms of compounds of formula I in all ratios,

or a physiologically tolerable salt of a compound of formula I,

or a physiologically tolerable salt of a stereoisomeric form of a compound of formula I.

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